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# Evaluation of exogenous glucocorticoid injection on preweaning growth performance of neonatal pigs under commercial conditions<sup>1,2</sup>

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**ABSTRACT:** Three commercial trials were conducted to evaluate the use of dexamethasone (Dex) and/or isoflupredone (Predef) in improving preweaning growth performance of neonatal pigs. The objectives of the commercial trials were threefold: 1) to evaluate Predef in comparison with Dex; 2) to address the sexual dimorphic growth response observed in a previous commercial trial; and 3) to determine whether there is any benefit of providing Dex treatment to pigs being fed supplemental milk. In Exp. 1, 276 pigs (Triumph 4 × PIC Camborough 22) were assigned according to birth weight and sex to three treatments. Treatments included saline (Control), Dex (2 mg/kg BW i.m. injection of Dex), or Predef (2 mg/kg BW i.m. injection of Predef 2X) within 24 h after birth. A treatment effect was observed for BW at weaning ( $P < 0.001$ ), with pigs injected with Predef being 0.51 kg lighter than Control and Dex-treated pigs. The lower BW of Predef-treated pigs at weaning were a result of a lower ADG ( $P < 0.001$ ) during the preweaning period compared with Control

and Dex pigs. In Exp. 2, 703 pigs (Triumph 4 × PIC Camborough 22) were assigned according to birth weight and sex to three treatments. Treatments included either an i.m. injection of saline (Control), Dex1 (1 mg/kg BW of Dex), or Dex2 (2 mg/kg BW of Dex) within 24 h after birth. No treatment effects were observed for BW at weaning ( $P = 0.24$ ) or ADG ( $P = 0.19$ ). In Exp. 3, 342 pigs (Genetiporc) were assigned according to birth weight and sex to two treatments. Treatments included either an i.m. injection of saline or Dex (2 mg/kg BW) within 24 h after birth. All pigs were provided supplemental milk from the time of treatment until weaning age. No treatment effects were observed for BW at weaning ( $P = 0.13$ ) or ADG ( $P = 0.11$ ). The negative response to Predef was similar to the growth-suppressive effects observed by others using chronic glucocorticoid treatment. In contrast to our previous findings, Dex did not improve preweaning growth performance regardless of dose or supplemental milk.

Key Words: Glucocorticoids, Growth, Pigs

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## Introduction

Recently, it was reported that dexamethasone (a synthetic glucocorticoid) given to baby pigs within 1 h of birth increases weaning weight compared with pigs not injected with dexamethasone (Carroll, 2001; Seaman-Bridges et al., 2003). Furthermore, dexamethasone given to baby pigs within 24 h of birth increased wean-

ing weight, and the beneficial growth effects associated with Dex treatment persisted until market age (Gaines et al., 2002).

To date, there have been no attempts in neonatal pigs to determine whether Predef (a potent synthetic glucocorticoid) elicits growth-promoting effects similar to those observed with dexamethasone. However, it has been shown that Predef improves growth performance in weaned pigs compared with dexamethasone (Gaines et al., 2003). Sexual dimorphic responses have also been observed with dexamethasone treatment in neonatal pigs, with enhanced growth in males but not females (Gaines et al., 2002). This observation suggests differences in glucocorticoid sensitivity in the male and female pig. Furthermore, it has been suggested that preweaning growth of dexamethasone-treated pigs is driven by higher intakes of both colostral proteins and/or total milk (Carroll, 2001; Gaines et al., 2002). In any case, if dexamethasone treatment stimulates food intake in the neonatal pig, then the magnitude of the

<sup>1</sup>Mention of a trade name or proprietary product does not constitute a guarantee or warranty of the product by the USDA and does not imply its approval to the exclusion of other products that may also be suitable.

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growth response will most likely depend on sow milk output. Therefore, in instances where milk output may be limiting (i.e., during heat stress), supplemental milk replacer may need to be supplied. Therefore, the objectives of the commercial trials we conducted were three-fold: 1) to evaluate Predef compared with dexamethasone; 2) address the sexual dimorphic growth response observed in a previous commercial trial; and 3) to determine whether there is any benefit of providing dexamethasone treatment to pigs being fed supplemental milk.

## Materials and Methods

### Experiment 1

This experiment was conducted at a 1,800-sow commercial production unit. For this experiment, 276 pigs (Triumph 4 × PIC Camborough 22) were used from primiparous and multiparous sows. To avoid the confounding effects of parity and/or litter, pigs were randomly assigned within the litter by birth weight and sex to one of three treatments. Treatments included an i.m. neck injection of sterile saline (Control), dexamethasone solution (Phoenix Pharmaceuticals, Inc., St. Joseph, MO) at 2 mg/kg BW within 24 h of birth (**Dex**), or isoflupredone solution (Predef2X; Pharmacia Upjohn Co., Kalamazoo, MI) at 2 mg/kg BW within 24 h of birth (**Predef**). Dosage was determined by weighing the pig immediately before injection. After receiving either the saline or glucocorticoid injection (Dex or Predef) pigs were processed according to routine management practices, which included tail docking and i.m. iron dextran injection (200 mg/pig). For this study, all pigs were ear-notched for identification. Male pigs were castrated on d 5 after farrowing. All pigs were cross-fostered within the 24 h before treatment and remained within their respective litter until termination of the experiment. All sows received an i.m. injection of 5 mg of dinoprost tromethamine (Lutalyse; Pharmacia Upjohn Co.) at 113 d of pregnancy to synchronize parturition. For all treatments, pigs were individually weighed at weaning ( $17 \pm 1$  d).

### Experiment 2

This experiment was conducted during the spring at a 5,500-sow commercial production unit. For this experiment, 703 pigs (Triumph 4 × PIC Camborough 22) were used. Because this commercial sow unit was relatively new, pigs were used from first- or second-parity sows. To avoid the confounding effects of parity and/or litter, pigs were randomly assigned within the litter by birth weight and sex to one of three treatments. Treatments included either an i.m. neck injection of sterile saline (Control), dexamethasone solution (Phoenix Pharmaceuticals, Inc., St. Joseph, MO) at 1 mg/kg BW within 24 h of birth (**Dex1**), or dexamethasone at 2 mg/kg BW within 24 h of birth (**Dex2**). Pigs were

assigned to their respective treatments within 24 h after birth. Dosage was determined by weighing the pig at this time. All sows received an i.m. injection of 5 mg of Lutalyse (Pharmacia Upjohn Co.) at 113 d of pregnancy to synchronize parturition. If the sows had not initiated farrowing 24 h later, then 0.5 mL (20 IU/mL) of oxytocin was administered intramuscularly. At the time of birth, piglets were placed into survivability boxes to prevent hypothermia. Survivability boxes were plastic containers with wood shavings and a heat lamp. Pigs were kept in these boxes for a period of approximately 30 min before they were returned to the sow. All pigs were cross-fostered within the 24 h before treatment. Pigs were processed according to routine management practices that included tail docking, castration, and i.m. iron dextran injection (200 mg/pig). For this study, all pigs were ear-notched for identification. After receiving either the saline or the dexamethasone injection, pigs were processed and remained within their respective litter until termination of the experiment. For all treatments, pigs were individually weighed at weaning ( $13 \pm 1$  d).

### Experiment 3

This experiment was conducted during early summer at a 1,300-sow commercial production unit. For this experiment, 342 pigs (Genetiporc) were used from primiparous and multiparous sows. To avoid the confounding effects of parity and/or litter, pigs were randomly assigned within the litter by birth weight and sex to two treatments. Treatments included either an i.m. neck injection of sterile saline (Control) or dexamethasone solution (Phoenix Pharmaceuticals, Inc.) at 2 mg/kg BW within 24 h of birth (Dex). Pigs were assigned to their respective treatments within 24 h after birth. Dosage was determined by weighing the pig at this time. All sows received an i.m. injection of 263 µg of cloprostenol sodium (Estrumate Schering-Plough, Kenilworth, NJ) at 113 d of pregnancy to synchronize parturition. If the sows had not initiated farrowing 24 h later, then 0.5 mL (20 IU/mL) of oxytocin was administered intramuscularly. At the time of birth, piglets were placed into survivability boxes as for Exp. 2. All pigs were cross-fostered within the 24 h before treatment. After receiving either the saline or dexamethasone injection, pigs were processed according to routine management practices that included teeth clipping, tail docking, castration, and i.m. iron dextran injection (200 mg/pig). Pigs were also provided ad libitum access to supplemental milk until the time of weaning. Male pigs were castrated on d 3 after farrowing. For purposes of this study, all pigs were ear-notched for identification. Pigs remained within their respective litter until termination of the experiment. For all treatments, pigs were individually weighed at weaning ( $15 \pm 1$  d).

### Statistical Analyses

For all experiments, birth and wean weights were subjected to ANOVA using the GLM procedure of SAS

**Table 1.** Effect of glucocorticoid injection on BW from birth until weaning (Exp. 1)<sup>a</sup>

Variable	Control	Dex	Predef	SEM	Barrow	Gilt	SEM	Trt	Sex	Trt × Sex
No. of pigs	91	95	90	—	135	141	—	—	—	—
Mortality, %	9.18	6.29	7.78	0.03	11.24	4.26	0.02	0.34	0.03	0.62
Birth wt, kg	1.54	1.54	1.51	0.03	1.56	1.50	0.02	0.43	0.27	0.64
Weaning wt, kg	4.82 <sup>b</sup>	4.82 <sup>b</sup>	4.31 <sup>c</sup>	0.10	4.64	4.65	0.08	<0.001	0.92	0.70
ADG, g	200.7 <sup>b</sup>	202.0 <sup>b</sup>	170.1 <sup>c</sup>	5.93	189.7	192.2	4.90	<0.001	0.71	0.65

<sup>a</sup>Data are least squares means for each treatment. Pigs were weaned at  $17 \pm 1$  d of age. Barrows and gilts were injected with dexamethasone (2 mg/kg BW; Dex), isoflupredone (Predef), or injected with sterile saline (Control) within 24 h after parturition.

<sup>b,c</sup>Means within the main effect of treatment and within a row that do not have a common superscript differ ( $P < 0.05$ ).

(SAS Inst., Inc., Cary, NC), and least squares means comparisons were made using Fisher's protected least significant difference. The statistical model included effects of birth treatment, litter, sex, and interactions, with pig as the experimental unit.

## Results

Data for Exp. 1 are presented in Table 1. Birth weights ( $1.53 \pm 0.02$  kg) did not differ among treatments ( $P = 0.43$ ) or between sexes ( $P = 0.27$ ). A treatment effect was observed for BW at weaning ( $P < 0.001$ ) with pigs injected with Predef being 0.51 kg lighter than Control or Dex-treated pigs. In addition, a treatment effect was observed for ADG, with Predef-treated pigs having a lower ADG ( $P < 0.001$ ) than Control or Dex-treated pigs. There were no differences at weaning between Dex and Control pigs for ADG or BW. Additionally, no sex differences were observed for BW or ADG at weaning and no treatment differences were observed for preweaning mortality. A sex effect was observed for preweaning mortality ( $P = 0.03$ ) with over a two-fold higher mortality rate in male pigs. The average mortality rate for the overall period was 7.75%.

Data for Exp. 2 are presented in Table 2. Birth weights ( $1.69 \pm 0.01$  kg) did not differ among treatments ( $P = 0.78$ ) or between sexes ( $P = 0.09$ ). No treatment effects were observed for BW or ADG at weaning. There was no sex effect for BW at weaning or ADG from birth through weaning. No treatment differences were observed for mortality; however, there was a sex effect ( $P = 0.03$ ) with barrows having nearly a twofold higher

mortality rate than the gilts during the preweaning period. The average mortality rate for the overall period was 8.0%.

Data for Exp. 3 are presented in Table 3. Birth weights ( $1.58 \pm 0.03$  kg) did not differ among treatments ( $P = 0.83$ ) or between sexes ( $P = 0.24$ ). No treatment effects were observed for BW or ADG at weaning. No treatment differences were observed for mortality rate during the preweaning period. Though it was not statistically significant, barrows had nearly a twofold higher mortality rate than the gilts. The average mortality rate was 9.1%.

## Discussion

The responses to dexamethasone injection in the current experiments are inconsistent with earlier studies conducted in our laboratory. Carroll (2001) observed a 10.1% increase in BW at weaning (d 18) when pigs were administered dexamethasone (1 mg/kg BW) within 1 h of birth, which was accompanied by a substantially higher concentration of IGF-I. Similarly, Seaman-Bridges et al. (2003) observed a 22.3% increase in BW at weaning (d 18) when pigs were administered dexamethasone (1 mg/kg BW) within 1 h of birth. Furthermore, Gaines et al. (2002) in an experiment conducted at the same location as Exp. 1, observed a 10% increase in BW at weaning when pigs were given dexamethasone (2 mg/kg BW) within 24 h of birth. In the present study, Predef, which is a more potent glucocorticoid than dexamethasone, depressed piglet growth. This response is

**Table 2.** Effect of dexamethasone dosage on growth performance from birth until weaning (Exp. 2)<sup>a</sup>

Variable	Control	Dex1	Dex2	SEM	Barrow	Gilt	SEM	Trt	Sex	Trt × Sex
No. of pigs	238	233	232	—	365	338	—	—	—	—
Mortality, %	6.30	9.77	7.59	0.02	10.16	5.61	0.01	0.34	0.03	0.32
Birth wt, kg	1.69	1.69	1.68	0.02	1.71	1.67	0.02	0.78	0.09	0.59
Weaning wt, kg	4.65	4.62	4.59	0.06	4.64	4.59	0.05	0.24	0.22	0.87
ADG, g	230.6	225.8	226.4	3.86	229.0	226.2	3.14	0.19	0.43	0.88

<sup>a</sup>Data are least squares means for each treatment. Pigs were weaned at  $13 \pm 1$  d of age. Barrows and gilts were injected with dexamethasone (1 mg/kg BW; Dex1), dexamethasone (2 mg/kg BW; Dex2), or injected with sterile saline (Control) within 24 h after parturition.



**Table 3.** Effect of dexamethasone on pig growth performance from birth until weaning with supplemental milk replacer (Exp. 3)<sup>a</sup>

Variable	Control	Dex	SEM	Barrow	Gilt	SEM	Trt	Sex	Trt × Sex
No. of pigs	169	173	—	165	177	—	—	—	—
Mortality, %	9.62	8.71	0.02	12.14	6.19	0.02	0.69	0.20	0.17
Birth wt, kg	1.58	1.58	0.03	1.61	1.55	0.03	0.83	0.24	0.96
Weaning wt, kg	5.09	4.92	0.09	5.13	4.87	0.09	0.13	0.12	0.61
ADG, g	229.4	218.1	5.28	228.3	219.2	5.28	0.11	0.28	0.56

<sup>a</sup>Data are least squares means for each treatment. Pigs were weaned at  $15 \pm 1$  d of age. Barrows and gilts were injected with dexamethasone (2 mg/kg BW; Dex), isoflupredone (Predef), or sterile saline (Control) within 24 h after parturition. All pigs had ad libitum access to supplemental milk replacer from 24 h after birth until weaning.

similar to the effects observed with chronic glucocorticoid administration.

In earlier studies, it has been shown that chronic dexamethasone treatment suppresses growth in neonatal pigs (Weiler et al., 1997; Burrin et al., 1999). Weiler et al. (1997) reported that long-term dexamethasone (0.5 mg/kg BW) administration to 7-d-old pigs for 15 d resulted in decreased piglet growth and increased protein catabolism. Burrin et al. (1999) also reported that chronic administration of dexamethasone (1 mg/kg BW) to 2-d-old pigs for 7 d reduced piglet growth rate and intestinal growth via increased protein catabolism. To our knowledge, this was the first experiment to evaluate preweaning growth performance of pigs injected with Predef. Therefore, we chose to administer Predef at a dose similar to dexamethasone, which we have evaluated extensively. However, based on the current study, we speculate that Predef bioactivity resulted in symptoms of glucocorticoid excess. Thus, the inconsistencies reported among studies with regard to the effects of glucocorticoids on postnatal growth arise from the dissimilarities associated with the duration (acute vs. chronic) of glucocorticoid exposure. Since there are obvious differences in glucocorticoid activity between dexamethasone and Predef, further studies need to be conducted evaluating dose responses to these exogenous glucocorticoids.

Due to the potential differences in glucocorticoid sensitivity, we evaluated graded levels of dexamethasone (0, 1, and 2 mg/kg BW). These concentrations were chosen because of the positive growth responses observed in previous studies (Carroll, 2001; Gaines et al., 2002; Seaman-Bridges et al., 2003). However, in Exp.2, we did not detect any improvement in preweaning growth performance at either concentration. As previously mentioned, this commercial sow unit was relatively new; the oldest sows were second parity and each litter contained 10 to 14 pigs. Thus, if dexamethasone improves preweaning growth performance by increasing food intake, then milk availability could have been limiting in this study as well as in Exp.1. As previously mentioned, Exp.1 was conducted at the same facility where we had conducted a previous study and observed a positive growth response to dexamethasone with the

only exception being season of the year. Interestingly, growth rates were quite different between the studies.

In the previous study, dexamethasone treated pigs (barrows) grew at an average rate of 224.4 g/d, whereas in the present study dexamethasone treated pigs (barrows) grew at an average rate of 198.9 g/d. These differences were not attributed to age since pigs were weaned at similar ages. However, the differences could be partially explained by differences in sow milk output since piglet growth rate is almost entirely dependent on both colostrum and milk availability. This fact is supported by the work of Noblet and Etienne (1987), in which preweaning growth was strongly related to sow milk output ( $r^2 = 0.87$  to  $0.90$ ). The causative factor for the decrease in sow milk output is not clear in the present study; however, it points to the fact that the magnitude of the growth response to dexamethasone is most likely dependent on milk availability since glucocorticoids have been shown to stimulate food intake in young pigs (Gaines et al., 2003). Therefore, in instances where milk output may be limiting (i.e., during heat stress), supplemental milk replacer may need to be supplied. However, when we supplied milk replacer to dexamethasone-treated pigs during a period of heat stress, we still did not observe differences in growth performance.

Based on the responses observed in the current experiments, there seems to be no benefit of treating neonatal pigs with dexamethasone to improve preweaning growth performance. These responses are inconsistent with our earlier studies demonstrating improvements in preweaning growth performance with dexamethasone treatment. It is important to point out that our earlier studies were all conducted in a controlled laboratory setting with the exception of one experiment that was conducted in a commercial production unit. With this in mind, there may be the potential for other “stressors” within a commercial production unit that could mimic the potential appetite/growth stimulating effects of dexamethasone treatment.

Gallagher et al. (2002) reported that piglets handled frequently for saliva sampling were heavier at weaning on d 28 compared with those treated only with routine commercial interventions, an observation seen by these researchers in a previous study. In contrast, Weaver et

al. (2000) reported that neonatal handling of boars had permanent effects on hypothalamic pituitary axis function, with handled boars having increased plasma corticosteroid-binding and lower basal total and free plasma cortisol concentrations. Concomitant with the alterations in the HPA axis function was the observation that handled boars had decreased BW compared with boars that were not handled. The dichotomy between the studies may have been related to the frequency and duration of handling. In both cases, it was obvious that in neonatal pigs, there is not a period where pigs are not responsive to stress. This is supported by observations by Klemcke and Pond (1991), where plasma cortisol concentrations in young piglets could be elevated fourfold with maternal deprivation from 3 to 31 d of age. In Exp. 2 and 3, pigs were placed in survivability boxes in an effort to prevent hypothermia. However, this management practice could have interrupted our normal observations seen with dexamethasone since pigs were kept away from the sow for up to 30 min. Thus, it becomes very important when evaluating the growth-promoting effects of exogenous glucocorticoids, such as dexamethasone, that one is aware of external stimuli that may influence the expected response.

### Implications

Although the data for the present experiments are inconsistent with responses observed earlier in our laboratory, they suggest that other factors may influence the response to dexamethasone. The negative response to Predef was similar to the growth-suppressive effects observed with chronic glucocorticoid treatment. Further studies are warranted to evaluate the dose re-

sponse of both Predef and dexamethasone because there are obvious sensitivities in the synthetic analogs.

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